



JOHNS HOPKINS  
M E D I C I N E

# Taming the Opioid Epidemic: The Role of Naloxone Prescribing

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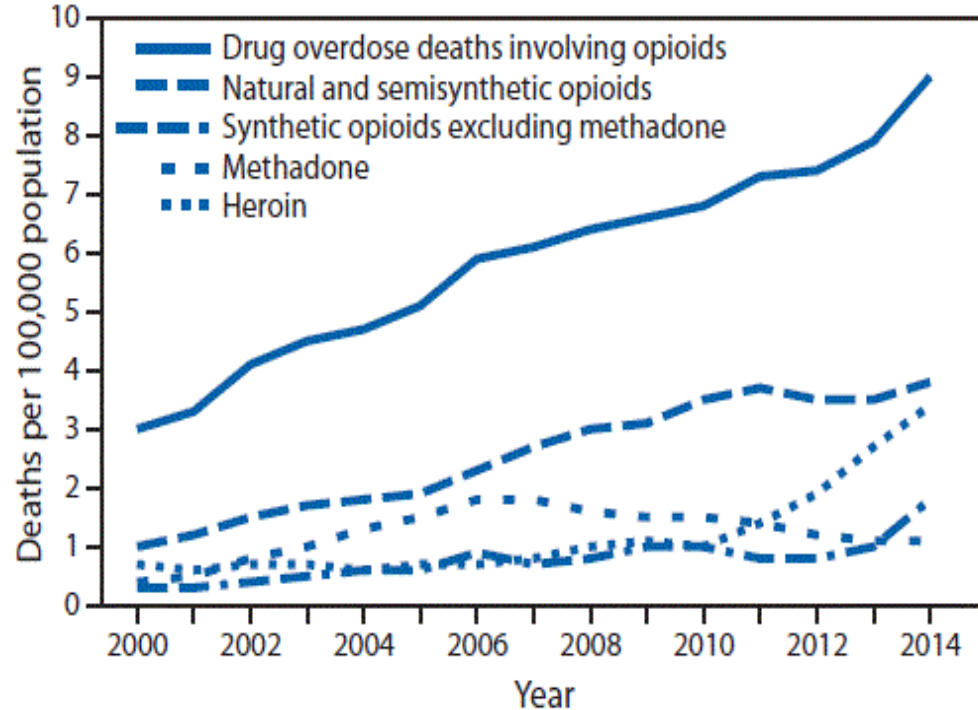
# Learning Objectives

- Evaluate currently available methods used to identify patients at high risk for opioid overdose
- Provide recommendations to aid providers in determining high-risk patient populations as well as writing and filling of naloxone prescriptions

# Learning Objectives (cont.)

- Compare strategies for incorporating opioid overdose education and naloxone programs into different health care practice settings
- Discuss challenges to developing and implementing naloxone prescribing in a health care system

# Drug Overdose Deaths Involving Opioids – US, 2000-2014



# History of Layperson Naloxone Distribution

- First reported in 1996
  - Overdose prevention community-based offered naloxone to laypersons who might witness an overdose
- From 1996 through 2014: CDC surveyed 136 organizations distributing or prescribing naloxone
  - 152,283 laypersons provided kits
  - 6,463 reversals reported

# Expanding Access to Naloxone

- According to a survey in 2014 performed by the CDC, **183%** increase in organizations providing/prescribing naloxone to laypersons from 2010


# Public Health Response: Naloxone Distribution


- Part of a public health mission
- Goal to prevent morbidity, mortality, and/or disease transmission
- Naloxone kits often dispensed without regard for reimbursement or 3<sup>rd</sup> party payment
  - Prior to FDA approval of outpatient products

# Medical Association Support

AMA Statement on Naloxone Product Approval

For immediate release:  
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 **American Association of Poison Control Centers**

 **ASAM**  
American Society of Addiction Medicine

Public Policy Statement  
Prevention of Drug

**YOU CAN STOP OVERDOSE DEATH**

**GET NALOXONE SAVE A LIFE**

<http://www.ama-assn.org/ama/pub/news/news/2014/2014-04-07-naloxene-product-approval.page>; [www.dontdie.org](http://www.dontdie.org);  
[http://www.acmt.net/Library/Press\\_Releases/Naloxone\\_Clinical\\_Toxicology\\_Release\\_10\\_08\\_14.pdf](http://www.acmt.net/Library/Press_Releases/Naloxone_Clinical_Toxicology_Release_10_08_14.pdf) ;  
<http://prescribetoprevent.org/wp2015/wp-content/uploads/1naloxone-rev-8-14.pdf>



# Project Lazarus

- Established 2008 Wilkes County, NC
- Community coalition
- Physician education
- Obtaining a naloxone kit

# Clinical Questions

1

- Do OOPPs with naloxone distribution reduce fatal and nonfatal overdose rates among participants?

2

- Are OOPPs effective at increasing nonmedical bystander knowledge of prevention, risk factors, and recognition of opioid overdose?

3

- Do nonmedical bystanders trained at OOPPs respond correctly to witnessed opioid overdoses?

OOPP: Opioid Overdose Prevention Program

Providing/prescribing naloxone to laypersons reduces overdose deaths, is safe, and is cost-effective.

# Is naloxone safe?

- Naloxone: displaces the opioid agonist from the mu receptor, reversing opioid induced respiratory depression (the primary clinical indication)
- Primarily administered in a healthcare setting, however use by laypersons is increasing
- Adverse effects: victim's increased annoyance, precipitation of opioid withdrawal, and acute respiratory distress syndrome (rare)

# Does naloxone reduce overdose deaths?

- Layperson naloxone administration has been identified as a safe, effective, and economical method to prevent death due to opioid overdose
- Administration of naloxone by bystanders is reported in over a dozen feasibility studies with reversal rates ranging from 75% to 100%

Coffin, P. *Annals of internal medicine* 158.1 (2013): 1–9.

Coffin, P. *Journal of medical economics* 16.8 (2013): 1051–1060; Piper T M. *Subst Use Misuse* 2008; 43: 858– 870; Enteen L. *J Urban Health* 2010 ; 87 : 931 – 941.; Loimer N. *J Psychiatr Res* 1992 ; 26 : 39 – 43 .

## Does naloxone reduce overdose deaths? (cont.)

- One study reported a reduction in mortality rates from 46.6 to 29.0 per 100,000 population
- Another study reported adjusted death rate ratios of 0.73 (with a 95% confidence interval of 0.57 – 0.91) in the implementation group versus the non-implementation group

# Limitations of Naloxone Studies

- Selection bias
- Information bias
- Lack of adequate, well-designed trials



# Is naloxone cost-effective?

- According to cost effectiveness study, 101 kits would need to be given out to prevent one overdose death
- Even if the most limited effects of naloxone are assumed and include costs related to criminal justice and other services for those heroin users who survive, naloxone distribution is a remarkably **inexpensive** way to save lives



# Why prescribe naloxone?

- We as health care providers must invoke the **precautionary principle**
  - A principle that seeks to implement preventative measures to respond to a real risk in the face of uncertainty regarding a tradeoff between safety concerns, efficacy, and cost issues

# WHO WILL BENEFIT MOST FROM NALOXONE?



# Risk Stratification: RIOSORD

- Risk index for overdose or serious opioid-induced respiratory depression (RIOSORD)
- Case control analysis of Veteran's Health Administration data
- 1.8 million patients with pharmacy record and opioid prescriptions
- 15 variables most highly associated with overdose or respiratory depression
- For risk assessment of medical users of prescriptions of opioids

Risk Factor (Yes/No?)	RIOSORD Score
<b>Does the patient have any of the following conditions?</b>	
Opioid Dependence	15
Chronic hepatitis or cirrhosis	9
Bipolar or schizophrenia	7
Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)	5
Chronic kidney disease with clinically significant renal impairment	5
An active traumatic injury, excluding burns (e.g., fracture, dislocation, contusion, laceration, wound)	4
Sleep apnea	3
<b>Does the patient consume the following medications?</b>	
An extended-release or long acting (ER/LA) formulations of any prescription opioid or opioid with long and/or variable half-life (e.g., OxyContin, Oramorph-SR, methadone, fentanyl patch)	9
Methadone	9
Oxycodone	3
A prescription anti-depressant	4
A prescription benzodiazepine	7
<b>What is the patient's current maximum prescribed opioid dose (Oral Morphine Equiv.)</b>	
≥ 100 mg	16
50 – 99 mg	9
20-49 mg	5
<b>In the past 6 months, has the patient:</b>	
Had one or more emergency department visits	11
Been hospitalized for one or more days	8

# JHH Risk Factor Assessment

- Based upon literature review
- Individual risk factor assessment
- Recommended that all patients are screened for risk factors
- Can be applied throughout different care settings – quick and simple
- Two distinct patient populations
  - Active substance use disorder
  - Medication safety perspective



# Risk Factors – High Risk

- Active substance use disorder
- Emergency medical care for opioid overdose
- Discharge from opioid detoxification in the past 30 days
- Daily opioid doses exceeding 100 mg of oral morphine equivalents
- Release from incarceration with a history of a substance use disorder

# Risk Factors – Moderate Risk

- Controlled substance prescriptions from multiple pharmacies and prescribers
- Comorbid psychiatric disorders
- History of opioid addiction disorder
- Concurrent use of other CNS depressants
- Comorbid renal or hepatic dysfunction or respiratory diagnoses



# Methods of Procurement for Outpatient Naloxone

Overdose  
Response  
Programs

Third Party  
Prescribing

Patient –  
Prescriber  
Relationship

Standing  
Orders



# Naloxone Kit Examples





Left: <http://harmreduction.org/issues/overdose-prevention/tools-best-practices/od-kit-materials/>  
Right: <http://www.tulalipnews.com/wp/2014/11/20/naloxone-kits-now-available-in-snohomish-county/>



# Prescribing Naloxone

- Risk Factor Assessment
- Discussion with patient
  - Patient preference
  - Insurance Coverage
- Formulation Selection
- Patient Education

# Formulations of Naloxone Currently Available

Formulations	Comments	Cost and Insurance Information
<p><b>Intramuscular 0.4 mg</b></p> 	<ul style="list-style-type: none"><li>• Requires assembly and drawing up medication from vial</li><li>• Often not preferred by patients</li></ul>	<ul style="list-style-type: none"><li>• Cash price: \$\$</li><li>• Often covered by insurance</li><li>• Syringes and needles may be an additional cost</li></ul>
<p><b>Intranasal 2 mg</b></p> 	<ul style="list-style-type: none"><li>• Requires assembly</li><li>• Easy administration</li></ul>	<ul style="list-style-type: none"><li>• Least expensive and often covered by insurance</li><li>• Cash price: \$\$</li><li>• Atomizer may be an additional cost</li></ul>

# Formulations of Naloxone (cont.)

Formulations	Comments	Cost and Insurance Information
<p data-bbox="291 303 556 339"><b>Intranasal 4 mg</b></p> 	<ul data-bbox="807 306 1168 470" style="list-style-type: none"><li>• Large 4 mg dose</li><li>• Easy to administer with no assembly required</li></ul>	<ul data-bbox="1242 306 1580 423" style="list-style-type: none"><li>• Cash price: \$\$\$</li><li>• Often covered by insurance</li></ul>
<p data-bbox="291 642 730 678"><b>Evzio® Auto injector 2 mg</b></p> 	<ul data-bbox="807 645 1168 809" style="list-style-type: none"><li>• Easy to use and auto injector provides verbal instructions for use</li></ul>	<ul data-bbox="1242 645 1632 809" style="list-style-type: none"><li>• Expensive and often not covered by insurance</li><li>• Cash price: \$\$\$\$\$</li></ul>

# INCORPORATION INTO HEALTH CARE SETTINGS

# Health Systems and Opioid Prescribing

- Recommend appropriate use of opioids inpatient and at discharge
  - Assessment and monitoring
  - Prescription drug monitoring programs
- Institute and uphold diversion deterrent policies and procedures
- Educate staff and patients about non-opioid treatments for pain

# Health Systems and Naloxone Prescribing

- Implement policies and procedures for risk factor assessment for opioid overdose
- Simplify prescription process
- Naloxone Prescribing Education
- Engage all health care professionals

# Community Practice

- Risk factor assessment
- Appropriate prescribing of opioids
- Open and honest conversation with patients about opioids
- Utilize opioid agreements and urine tox screens
- Create relationships with outpatient pharmacies
  - Staff used to dealing with 3<sup>rd</sup> party payers and obtaining prior authorizations
  - Have the medication on hand
  - Familiar with proper patient/caregiver education



# Naloxone Standing Orders

- A physician's order/prescription that can be carried out by other health care professionals when predetermined conditions have been met
  - Can be state-wide or city-wide
  - Predetermined conditions vary
- More than half of the US have naloxone standing order programs



## STANDING ORDER FOR BALTIMORE CITY PHARMACISTS

Pharmacists may dispense any of the following naloxone formulations.

**Check formulation dispensed:**

**Refill=PRN**

**Narcan:** Nasal Spray (4mg of naloxone hydrochloride in 0.1mL). 2 pack kit (up to 2 kits).

**Directions:** Spray into one nostril. May repeat x1, if no response after 3 minutes.

**Evzio:** Auto-injector (Naloxone 2 mg). 2 pack kit (up to 2 kits).

**Directions:** Use as instructed by device. May repeat x1, if no response after 3 minutes.

**Intranasal:** Naloxone (2mg/2mL) single dose Luer-Lock prefilled syringe. Qty= 2 or 4 syringes. Dispense with intranasal mucosal atomizer device.

**Directions:** Spray one-half of syringe (1 mL) into each nostril upon signs of opioid overdose. May repeat x1, if no response after 3 minutes.

For more information about naloxone visit [www.dontdie.org](http://www.dontdie.org).

For substance use treatment call the 24/7 Crisis, Information, and Referral Line: 410-433-5175.



Leana S. Wen, M.D., M.Sc., FAAEM  
Commissioner of Health, City of Baltimore

NR# 122527943

This prescription does not require completion of a specialized training in overdose recognition and response or possession of a training certificate.


# Challenges

- Billing
  - Insurance vs. cash
- Availability
  - Shortage
  - Outpatient pharmacy inventory
- Route of administration
  - Intranasal or intramuscular
- Kits vs. commercial products
- Ensuring prescriptions are filled
- Stigma

# Challenges to Implementation across a Health System

- Consistency of patient assessment
  - History of opioid overdose vs medication safety
- Staff education
- Electronic prescribing
- Patient education
- Incorporation into discharge process

# Paper Prescribing

 <p>JOHNS HOPKINS MEDICINE THE JOHNS HOPKINS HOSPITAL</p>	Date: _____ Patient Name: _____ DOB: _____ Weight (Pediatrics): _____ Address: _____
May auto-substitute other formulation / kit based upon insurance coverage.	
<input type="checkbox"/> <b>INTRAMUSCULAR KIT</b> Rx: Naloxone Intramuscular Kit Naloxone Injection 0.4 mg/1 mL vial x 2 3 cc, 23 g, 1 inch syringes with needle x 2 Alcohol Pad x 2	Qty: 1 Naloxone Intramuscular Kit Refill: PRN Sig: For suspected opioid overdose, inject 1 mL of naloxone into the shoulder or thigh muscle, may repeat after 3 minutes if no or minimal response.
<input type="checkbox"/> <b>INTRANASAL KIT (Total Dose: 2 mg)</b> Rx: Naloxone Intranasal Kit Naloxone 2 mg/2 mL single-dose Luer-jet prefilled syringe x 2 Intranasal mucosal atomizer device x 2	Qty: 1 Naloxone Intranasal Kit Refill: PRN Sig: For suspected opioid overdose, spray 1 mL of naloxone in each nostril, may repeat after 3 minutes if no or minimal response.
<input type="checkbox"/> <b>NASAL SPRAY (Total Dose: 4 mg)</b> Rx: NARCAN® 4 mg/0.1 mL nasal spray	Qty: 1 box (2 count) Refill: PRN Sig: For suspected opioid overdose, administer a single spray of nasal spray in one nostril, may repeat after 3 minutes if no or minimal response.
<input type="checkbox"/> <b>AUTONJECTOR</b> Rx: Evzio® auto-injectors (Naloxone 0.4 mg per injection)	Qty: 1 box (2 count) Refill: PRN Sig: For suspected opioid overdose, use as directed. May repeat x 1 dose, if no or minimal response after 3 minutes.
PHYSICIAN NAME: _____	
PHYSICIAN SIGNATURE: _____	
NPI#: _____	
Security Features: Prints "VOID" on front when duplicated - Green background highlights assure alterations - Watermark on back can be seen when held at 90° on an angle - Covert reactive ink on watermark changes color when scratched with a coin - Heat-sensitive ink on back disappears when subject to heat or touch - Microtext print contains the DocuGuard name and is difficult to copy - Security Features describe tamper-resistant attributes.	
NC-9 (5/16)	

# e-Prescribing

## Naloxone for overdose <sup>⌆</sup>

Please choose one formulation based upon patient preference and insurance coverage.

1. Most commercial insurances and Maryland Medicaid cover all the formulations except the auto-injector without prior authorization.
2. Narcan® nasal spray (4 mg/0.1mL) is generally preferred because of ease of administration and insurance coverage.
3. Prescription includes auto-substitution statement in case insurance does not cover originally prescribed option.

naloxone (NARCAN) 4 mg/actuation nasal spray

Disp-1 each, R-3, May Sub: Naloxone 1mg/mL IN kit: 1mL in each nostril \* Disp 4mL w/2 atomizers OR Naloxone 0.4mg/mL IM Kit: 1mL in shoulder/thigh \* Disp 2mL w/2 3 mL syringes & 2 1" needles \* = PRN Repeat if no response in 3 min

naloxone (NARCAN) 1 mg/mL intranasal Kit

Disp-4 mL, R-3, May sub: Narcan Nasal Spray(4mg): 1 spray into one nostril \* Disp 1 box OR Naloxone 0.4mg/mL IM Kit: 1mL in shoulder/thigh \* Disp 2mL w/two 3 mL syringes & two 1" needles. \* = PRN Repeat if no response in 3 min

naloxone (NARCAN) 0.4 mg/mL injection (KIT)

Disp-2 mL, R-3, May sub: Narcan Nasal Spray(4mg): 1 spray into one nostril \*. Disp 1 box -OR- Naloxone 1mg/mL IN kit: 1mL in each nostril \*. Disp 4mL w/ 2 atomizers. \* = PRN Repeat if no response in 3 min

naloxone (EVZIO) 0.4 mg/0.4 mL auto-injector

Disp-2 Syringe, R-3, May sub: Naloxone 1mg/mL IN kit:1mL in each nostril \*. Disp 4mL w/2 atomizers -OR- Narcan Nasal Spray(4mg): 1 spray into one nostril \*. Disp 1 box. \* = PRN Repeat if no response in 3 min

# Patient Education

- Two different patient populations
- Numerous formulations
- Creating simple and appropriate handouts
- “Patient-friendly”
- Visually appealing

# Patient and Family Advisory Councils

- Diverse councils composed of patients, caregivers, family members, and hospital employees
- Adult and pediatric councils
- Emergency Department Council
- Invaluable feedback



#### Good Samaritan Law

Maryland has a Good Samaritan Law. Callers to 911 and persons who give naloxone are not liable and cannot be arrested, charged, or prosecuted for a good faith attempt to help someone.

#### Additional Resources

For more information about naloxone and preventing overdose:

[www.prescribtoprevent.org](http://www.prescribtoprevent.org)  
[www.dontdie.org](http://www.dontdie.org)

For information about Maryland State Overdose Response Programs and Certificate Training Programs, please visit:

[www.maryland.gov](http://www.maryland.gov) or call the Crisis Information and Referral line at 410-433-5153.

If you have additional questions, please contact your doctor or pharmacist.



Johns Hopkins Medicine  
Department of Pharmacy

## Naloxone (Narcan®) Information for Patients



#### What is naloxone?

Naloxone (nal-OX-one) is a medicine used to reverse an opioid (sometimes called narcotics) overdose.

#### What is a narcotic overdose?

It can be caused from using too many narcotic medicines. In some cases, these medicines can cause side effects such as sleepiness or trouble breathing.

Examples of narcotics:

- Morphine (MS Contin®)
- Hydrocodone (Vicodin®, Norco®)
- Hydromorphone (Dilaudid®)
- Oxycodone (Percocet®, Oxycotin®)
- Oxymorphone (Opana®)
- Fentanyl (Duragesic®)
- Buprenorphine (Suboxone®, Subutex®)
- Methadone (Dolophine®)
- Street drugs, such as: heroin

#### Who should get naloxone?

If someone has used a narcotic medicine and has one or more of the following signs of a narcotic overdose:

- Trouble breathing (gaspings)
- Breathing is very slow or has stopped
- Trouble waking up
- Skin is pale and/or clammy to the touch or fingernails and/or lips are blue/purple

#### How to decrease your risk of an overdose

- Take your medicines as prescribed by your doctor.
- Do not take narcotics in higher doses or more often than prescribed.
- Do not take other medicines that can cause sleepiness with narcotics without talking to your doctor or pharmacist first.
- Do not drink alcohol while taking narcotics.

#### Important Information

If someone is experiencing a narcotic overdose, you should:

- **Get help by calling 911 IMMEDIATELY**
- Give naloxone. Instructions are on the inside of this pamphlet.

**IMPORTANT:** Tell others where your naloxone is stored and how to use it.

**INSTRUCTIONS FOR GIVING  
 NALOXONE**


**1. Identify Overdose**—If a person is showing signs of narcotic overdose, try to wake them up by forcefully rubbing your fist up and down the middle of their chest.

**2. Call 911 Immediately**—Clearly state what you see (the person is not responding and not breathing) and the address and location of the person.

**3. Give Naloxone. See instructions →**

**4. Take care of the person**

a. If comfortable, you may give mouth-to-mouth breaths by tilting their head back slightly, pinching their nose, and giving 1 breath every 5 seconds.



b. Place them on their side if they wake up.

c. Be prepared to give **another dose** of naloxone. The effects will wear off in 15-30 minutes.

**5. Stay until help arrives.**

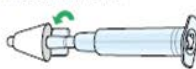
## Option A

### NASAL SPRAY NALOXONE

**1** Take off yellow caps.



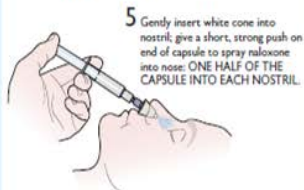
**2** Screw on white cone.



**3** Take plastic cap off capsule of naloxone.



**4** Gently screw capsule of naloxone into barrel of syringe.



**5** Gently insert white cone into nostril; give a short, strong push on end of capsule to spray naloxone into nose: **ONE HALF OF THE CAPSULE INTO EACH NOSTRIL.**

**6** If no reaction in 3 minutes, give second dose.



## Option B

### NASAL SPRAY NARCAN®

**1** Peel back the tab with the circle to open the NARCAN® Nasal Spray.



**2** Hold the NARCAN® Nasal Spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.



**3** Gently insert the tip of the nozzle into one nostril until your fingers on either side of the nozzle are against the bottom of the person's nose.

**4** Press the plunger firmly to give the dose of NARCAN® Nasal Spray.



**5** If no reaction in 3 minutes, give second dose.



## Option C

### INJECTABLE NALOXONE

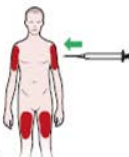
**1** Remove plastic cap from naloxone vial and uncover the needle.



**2** Insert needle through rubber plug with vial upside down. Pull back on plunger and take up 1 mL.



**3** Inject 1 mL of naloxone into upper arm or thigh muscle.



**4** If no reaction in 3 minutes, give second dose.



## Option D

### EVZIO® AUTO-INJECTOR

It contains a speaker that provides instructions to inject naloxone into the outer thigh, through clothing if needed.



# Key Takeaways

- Identification of individuals at risk and explanation of role of naloxone is key
- Implementing programs to facilitate naloxone prescribing in different health care settings can be challenging, but necessary because naloxone save lives
- Creating robust and effective educational plans for patients is vital to proper naloxone use

# Pain Symposium: Sept. 25, 2017

- Focused on opioid stewardship and pain management (inpatient and outpatient)
- Keynotes:
  - Boyd Rutherford, Md. Lt. Governor
  - Peter Pronovost, Armstrong Institute
- In-person and live-stream options

[hopkinsmedicine.org/armstrong/painsymposium](https://hopkinsmedicine.org/armstrong/painsymposium)

# Thank you!

For questions or follow-up, please contact:

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Juliana Zschoche, PharmD, BCPS: [jzschoc1@jhmi.edu](mailto:jzschoc1@jhmi.edu)

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